NCIC OPPT/DC/USEPA/US
Sent by: JuanB Perez

05/27/2005 01:31 PM

To NCIC HPV@EPA
cc
bcc
Subject Re: DMSO: FINAL SUBMISSION - Dimethyl Sulfoxide Under HPV Program

US Environmental Protection Agency
Office of Pollution Prevention and Toxics Docket
Non-Confidential Information Center (MC 7407T)
(operated by ASRC Aerospace Corporation)
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Washington DC 20460
phone 202-566-0280 * fax 202-566-0282 * e-mail oppt.ncic@epa.gov
Elizabeth Hunt <ehunt@adelphia.net>

Elizabeth Hunt
<ehunt@adelphia.net>
05/27/2005 01:07 PM

To NCIC OPPT@EPA, Rtk Chem@EPA
cc Ralph Northrop/DC/USEPA/US@EPA
Subject DMSO: FINAL SUBMISSION - Dimethyl Sulfoxide Under HPV Program

Resubmission :

This submission is being made on behalf of the DMSO Producers Association regarding its commitment to sponsor **DMSO (CAS Number 67-68-5)** under the HPV Program.

The dossier was sent to EPA following the first submission last year. If you need another copy, please advise where is should be sent.

This is the **FINAL** submission regarding this compound. ***Please post this on the EPA website*** .

If you have any questions, please contact me.

Elizabeth Hunt
Executive Director, DMSO Producers
941 Rhonda Place
Leesburg, VA 20175

-----Original Message-----
From: Elizabeth Hunt [mailto:ehunt@adelphia.net]
Sent: Wednesday, June 23, 2004 12:27 PM
To: 'Hefter.Richard@epamail.epa.gov'
Cc: 'Northrop.Ralph@epamail.epa.gov'
Subject: DMSO: EPA comments on the Dimethyl Sulfoxide HPV Challenge submission--RESPONSE TO COMMENTS

Mr. Hefter:

Attached please find the DMSO Producers Association's response to EPA comments regarding Dimethyl Sulfoxide.

Due to the size of the revised dossier, I will send a hard copy via Fedex.

If you have any questions, please contact me.

Elizabeth Hunt
Executive Director

-----Original Message-----
From: Hefter.Richard@epamail.epa.gov [mailto:Hefter.Richard@epamail.epa.gov]
Sent: Friday, February 13, 2004 5:43 PM
To: ehunt@adelphia.net
Cc: Northrop.Ralph@epamail.epa.gov
Subject: EPA comments on the Dimethyl Sulfoxide HPV Challenge submission

Dear Ms. Hunt:

Attached please find EPA's comments on the Dimethyl Sulfoxide submission to the Chemical RTK Challenge Program and a transmittal letter from Dr. Oscar Hernandez, Director of OPPT's Risk Assessment Division. These items will also be sent to you in hard copy and are expected to be posted on the Chemical RTK website in a few days.

(See attached file: SN245 EPA Comments 021304.wpd)(See attached file: SN#245 Letter.wpd)

ResponsetoEPACommentsDMSO.doc

The DMSO Producers Association's Response to EPA Comments Regarding Dimethyl Sulfoxide (marked in red)

EPA Comments on Chemical RTK HPV Challenge Submission: Dimethyl Sulfoxide

Summary of EPA Comments

The sponsor, the Dimethyl Sulfoxide (DMSO) Producers Association, submitted a cover letter and robust summaries to EPA for dimethyl sulfoxide (DMSO; CAS No. 67-68-5) dated August 12, 2003. EPA posted the submission on the ChemRTK HPV Challenge Web site on October 15, 2003.

EPA has reviewed this submission and has reached the following conclusions:

1. Physicochemical Properties. The submitted data for all endpoints are adequate for the purposes of the HPV Challenge Program.

2. Environmental Fate. The submitted data for photodegradation, stability in water, and fugacity are adequate for the purposes of the HPV Challenge Program. The submitted data for biodegradation are inadequate.

2. Health Effects. Adequate data are available for acute, repeated-dose, and developmental toxicity and chromosomal aberrations for the purposes of the HPV Challenge Program. EPA reserves judgement on adequacy of the data submitted for gene mutations and reproductive toxicity endpoints pending receipt of additional information. The submitter needs to address deficiencies in the robust summaries.

3. Ecological Effects. Adequate data are available for fish for the purposes of the HPV Challenge Program. The data submitted for algae and aquatic invertebrates may be acceptable on a weight-of-evidence basis; however, the submitter needs to provide missing information in the robust summaries to allow an independent evaluation. EPA also recommends that values generated by SAR modeling be provided as supporting information.

EPA requests that the submitter advise the Agency within 60 days of any modifications to its submission.

EPA Comments On The Dimethyl Sulfoxide Challenge Submission

Test Plan

General

In lieu of a test plan the submitter stated in the cover letter that no testing was necessary.

Physicochemical Properties (melting point, boiling point, vapor pressure, partition coefficient and water solubility)

The submitted data for all endpoints are adequate for the purposes of the HPV Challenge Program.
Environmental Fate (photodegradation, stability in water, biodegradation, fugacity)

The submitted data for photodegradation, stability in water, and fugacity are adequate for the purposes of the HPV Challenge Program.

Biodegradation. The submitted Japanese MITI test was run for only two weeks rather than the four weeks required in OECD 301C. Since dimethyl sulfoxide might have passed a four-week test, the submitted data are inadequate and the submitter needs to perform the test according to OECD TG 301.

Data available and summarized.

Health Effects (acute toxicity, repeated-dose toxicity, genetic toxicity, and reproductive/developmental toxicity)

Adequate data are available for acute, repeated-dose, and developmental toxicity and chromosomal aberrations for the purposes of the HPV Challenge Program. EPA reserves judgment on the adequacy of the data submitted for gene mutations and reproductive toxicity endpoints pending receipt of additional information. The submitter needs to address deficiencies in the robust summaries.

Repeated-dose toxicity. The submitter needs to include a robust summary for a 13-week repeated-dose inhalation study in rats (OECD TG 413) submitted for the reproductive toxicity endpoint.

Done

Genetic toxicity (gene mutations). Adequacy of the data submitted for this endpoint cannot be determined because none of the robust summaries provides information on positive and negative controls. The submitter needs to provide this information, which is required to evaluate the validity of the assays, in addition to addressing deficiencies noted in the Specific Comments section.

Done

Reproductive toxicity. A robust summary for a 13-week repeated-dose inhalation study in rats (OECD TG 413) submitted for this endpoint indicates that the highest concentration is a NOAEL for reproductive parameters (histopathology, estrous and sperm effects), and no robust summary is provided for this study under the repeated-dose toxicity section to report whether or not the highest concentration is also a NOAEL for systemic toxicity. Additional omissions include the group size, the method for generating the test atmosphere, the maximum attainable concentration, and the results for systemic toxicity. Adequacy of the study for the reproductive toxicity endpoint cannot be determined pending receipt of the missing information in the robust summaries.

A robust summary of the 90-day inhalation toxicity study used for reproductive end-points was added in section 5.4

Ecological Effects (fish, invertebrates, and algae)

The studies for invertebrates were shorter than the OECD Guideline-required duration of 48 hours, and the data submitted for algae were generated in studies that were shorter or longer than the OECD Guideline-required duration of 72 or 96 hours. However, the data for these two endpoints may be acceptable on a weight-of-evidence basis. The submitter needs to provide missing information in the robust summaries so that an independent evaluation can be made. In addition, EPA recommends that values generated by SAR modeling be provided to support the conclusion of low toxicity.

A recently published daphnia study has been added to the robust summaries. In addition, the ecosar modeling information has been added as weight of evidence that DMSO is of low toxicity to aquatic organisms.

Specific Comments on the Robust Summaries

Health Effects

Acute toxicity. Robust summaries for acute oral toxicity studies in rats and mice are missing a few pieces of information, including the method for calculating the LD_{50} and the results for clinical signs and mortality by sex and exposure level. In addition, the summaries do not indicate whether body weights were monitored.

The available informations have been added.

Repeated-dose toxicity. Missing information in a robust summary for an 18-month oral study in rhesus monkeys includes mortality by sex and the reference citation.

No data available in the original publication

In addition, the reported NOAEL (3300 mg/kg bw) and LOAEL (9900 mg/kg bw) do not match the test doses provided (990-2970-8910 mg/kg) in the summary.

The mistake was Corrected

Genetic toxicity (chromosomal aberrations). A robust summary for an *in vivo* cytogenicity assay (chromosomal aberration) in rats does not adequately describe time of exposure and criteria for evaluating results. In addition, an attachment tabulating the percentage of aberrant cells per animal per dose level (Kapp table 1.tif) is missing.

The time of exposure is not explicitly reported in the publication; probably the animals were sacrificed 24 hours after the last treatment.

Developmental toxicity. A robust summary for a developmental toxicity study in rats by oral on gestational days 6-15 (OECD TG 414) omits the vehicle (if used), the magnitude of body weight effects, and statistical analysis.

The vehicle (purified water) was mentioned in the robust summaries, Additional data have been added on body weight effects.

Ecological Effects

Algae. The submitter needs to provide, where missing, the pH, water hardness, and temperature for as many studies as possible, particularly the 96-hour algal study on *Skeletonema costatum*.

Invertebrates. The submitter needs to provide missing pH, water hardness, temperature, dissolved oxygen, and other pertinent information.

A recently published reliable study has been included in the robust summaries. This information was not available in the other publications.

Followup Activity